Social Networks and Incident Stroke Among Women With Suspected Myocardial Ischemia

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Objective: To describe the prospective relationship between social networks and nonfatal stroke events in a sample of women with suspected myocardial ischemia. Social networks are an independent predictor of all-cause and cardiovascular mortality, but their relationship with stroke events in at-risk populations is largely unknown. **Method:** A total of 629 women (mean age = 59.6 ± 11.6 years) were evaluated at baseline for cardiovascular disease risk factors as part of a protocol including coronary angiography; the subjects were followed over a median 5.9 years to track the incidence of cardiovascular events including stroke. Participants also completed the Social Network Index (SNI), measuring the presence/absence of 12 types of common social relationships. **Results:** Stroke events occurred among 5.1% of the sample over follow-up. More isolated women were older and less educated, with higher rates of smoking and hypertension, and increased use of cardiovascular medications. Women with smaller social networks were also more likely to show elevations (scores of ≥10) on the Beck Depression Inventory (54% versus 41%, respectively; $p = .003$). Relative to women with higher SNI scores, Cox regression results indicated that more isolated women experienced strokes at greater than twice the rate of those with more social relationships after adjusting for covariates (hazard ratio = 2.7; 95% Confidence Interval = 1.1–6.7). **Conclusions:** Smaller social networks are a robust predictor of stroke in at-risk women, and the magnitude of the association rivals that of conventional risk factors. **Key words:** social networks, coronary artery disease, women, prospective, stroke.

CAD = coronary artery disease; **SES** = socioeconomic status; **CVD** = cardiovascular disease; **WISE** = Women's Ischemia Syndrome Evaluation; **PCI** = percutaneous coronary intervention; **CABG** = coronary artery bypass graft; **SNI** = Social Network Index; **BDI** = Beck Depression Inventory; **HR** = hazard ratio.

INTRODUCTION

Stroke is a leading cause of morbidity and mortality in the US, trailing only coronary artery disease (CAD) as a specific cause of death (1–3). The burden of stroke is disproportionately carried by women, who account for >60% of total stroke deaths (3). Known risk factors for the development and prevention of stroke parallel those of CAD, including hypertension, diabetes, smoking, obesity, and dyslipidemia, among others (4–6). However, whereas the relationship between CAD and psychosocial factors such as low socioeconomic status (SES), depression, and social relationships is supported by a large empirical literature (7–11), specific associations between psychosocial factors and cerebrovascular disease (CVD) incidence are comparatively rare (12–16).

This study prospectively examined the relationship between social networks and stroke over a median 5.9-year follow-up interval among a clinical sample of women with suspected myocardial ischemia. Women completed a measure of social networks as part of a protocol including a coronary angiogram and a CVD risk factor assessment.

METHOD

Participant Recruitment and Entrance Criteria

Women were eligible for participation in the Women's Ischemia Syndrome Evaluation (WISE) study if they were >18 years and were referred for a coronary angiogram to evaluate suspected myocardial ischemia (16). The WISE study was designed to improve the understanding and diagnosis of ischemic heart disease in women. Exclusion criteria included major comorbidity compromising follow-up, pregnancy, contraindication to provocative diagnostic testing, cardiomyopathy, severe heart failure, recent myocardial infarction or revascularization procedures, significant valvular or congenital heart disease, and language barrier. Data for WISE were collected between 1996 and 2005. All participants provided written informed consent, and Institutional Review Board approval was obtained for all participating sites.

Measurement of CAD and Clinical Outcome Events

Quantitative analysis of coronary angiograms was performed at the WISE Angiographic Core Laboratory (Rhode Island Hospital, Providence, Rhode Island) by investigators blinded to all other subject data (17). Luminal diameter was measured at all stenoses and at nearby reference segments, using an electronic cine projector-based "cross-hair" technique (Vanguard Instrument Corporation, Melville, New York). A CAD severity score was also developed by assigning increasing points to increasing percent stenosis (0–19, 20–49, 50–69, 70–89, 90–98, 99–100), after adjusting for presence of collaterals (filling of the occluded vessel or its distal branches anterograde or retrograde via channels other than the original lumen). Lesion location was

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taken into account in the scoring, with more proximal lesions receiving higher weighting (18).

Women were contacted at 6 weeks post baseline and annually thereafter for a median of 5.9 years (25^{th} percentile = 2.5 years; 75^{th} percentile = 6.9 years) to track subsequent cardiovascular events. Follow-up consisted of a scripted telephone interview by an experienced nurse or physician who inquired about hospitalization, treatment, or occurrence of myocardial infarction, congestive heart failure, and stroke. In the event of death, a death certificate was obtained and reviewed by a blinded WISE physician for classifying the cause of death. Subtypes of stroke were not differentiated.

Cardiovascular Risk Factor Measurement

Major CVD risk factors in the WISE protocol included smoking (dichotomized as current versus former or never smokers), history of dyslipidemia, history of diabetes, history of hypertension, and waist circumference. Risk factors were assessed by physical examination (waist circumference), self-report (smoking), and diagnosis and treatment history (dyslipidemia, diabetes, hypertension). Women were also assessed for medications used for treatment of CVD risk factors, including aspirin, lipid lowering medications (statin and nonstatin agents), and cardiovascular medications (including angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, diuretics, and vasodilators). For analytic purposes, the multiple lipid and hypertension medications were simplified into a pair of dichotomous variables (i.e., separate yes/no variables for using lipid and cardiovascular medications). Active treatment in the latter categories was defined by use in the previous week. Physical measurements of blood pressure, blood glucose levels, and cholesterol were also collected, but the substitution of these measurements for treatment history reports made no differences in event analyses. The participants' reported education history was dichotomously coded to indicate less than high school graduate versus high school diploma or greater. Education is a stable measure of SES (19). Women's race was also coded dichotomously (0 = White, 1 = non-White). Only 1.2% of the sample identified themselves as other than African-American or White.

Psychosocial Measures

Participants' baseline responses to the Social Network Index (SNI) (20) were used to measure social networks. The SNI has been used to predict inflammation in the Framingham and Third National Health and Nutrition Examination Survey cohorts (21,22), and total mortality outcomes in WISE (23). The SNI collects information on 12 types of social relationships, including friends, employment, neighbors, marriage partners, belonging to a church, children, parents, in-laws, other relatives, class attendance (e.g., university), volunteer work, and group memberships. Scoring of the SNI produces a measure of social network diversity based on the presence or absence of each of the 12 relationship domains over a 2-week period, with scores ranging from 0 to 12.

Participants also completed the Beck Depression Inventory (BDI) to measure depression symptom severity (24). The BDI is a 21-item questionnaire that has been validated in many clinical populations and linked to poor CAD outcomes (8).

Statistical Analyses

Descriptive statistics, t tests, and χ^2 statistics were used to make comparisons of more versus less isolated women on CVD risk factors (smoking history, waist circumference, history of diabetes, dyslipidemia, and hypertension), demographic characteristics (age, ethnicity, education), angiographic CAD severity score, and BDI scores. We sequentially built Cox regression models to adjust for demographic factors, BDI scores, CVD risk factors, and CAD severity scores. To correct for skewing, angiographic CAD severity scores were log transformed before inclusion in the analyses.

We first computed hazard ratios (HRs) for social network scores in continuous form, followed by a secondary analysis using the SNI in categorical form using high and low scorers based on a median split (scores of >6 were above the median), wherein women with larger social networks served as the reference category. We chose a dichotomous breakdown to maintain acceptable sample sizes that would have been compromised with additional groups. For a more detailed graphical display of the SNI-stroke relationship, we also created quartile groups, corresponding to SNI scores in the ranges of 1 to 5, 6, 7 to 8, and 9 to 11 in this sample. In the hazard models, stroke-free participants were censored at their last completed follow-up date. Model fit and validation were assessed on a logistic model containing all covariates using the goodness-of-fit test (Hosmer-Lemeshow χ^2 statistic) and the Shrunken R^2 statistic. Assumptions of equal proportionality held for the Cox Regression models.

Finally, because the initial analyses indicated that the SNI-stroke relationship contained a nonlinear component, we also examined the SNI-stroke relationship by completing Cox regression models with both linear and nonlinear SNI components (including quadratic, cubic, exponential, power, inverse, S-curve, and logarithmic transformations). All analyses were completed, using SPSS version 12.0 (SPSS Inc., Chicago, Illinois), with the criterion for statistical significance set at .05.

RESULTS

A total of 936 women were enrolled in WISE. From this group, 297 subjects were enrolled before the initiation of the psychosocial battery that included the SNI and BDI. An additional 10 women were removed due to an absence of follow-up data, leaving a total of 629 participants available for analysis. Thirty-one nonfatal and one fatal stroke events (5.1% of sample) were reported over a median 5.9 years of follow-up. Women categorized by SNI scores differed systematically (Table 1). Women with lower SNI scores were significantly older, had lower education levels, and were in poorer health as documented by CVD risk factors. More isolated women also had higher rates of depression with 57% versus 43% reporting BDI scores of ≥ 10 ($p = .003$). Stroke occurred among 4.4% (17/290) of women without SNI data, and these women did not differ significantly from those with SNI scores on any risk factor listed in Table 1 (data not shown).

Medications were commonly prescribed for CVD risk factor management. A total of 46.4% reported using one or more cardiovascular medications, and usage rates were higher among more socially isolated women (56.7% versus 42%; $p = .008$). There were no differences between SNI groups on rates of aspirin use or use of lipid-lowering medications.

Social Networks and Stroke Events

Before covariate adjustment, the presence of each additional relationship on the SNI was associated with a 23% decrease in stroke risk (HR = 0.77; 95% Confidence Interval (CI) = 0.62–0.94). Church membership and "other friendships" (comprised of friends not linked to SNI item categories) had the strongest inverse relationships to stroke among the specific relationship domains measured by the SNI (unadjusted RR = 0.44, 0.45; 95% CI = 0.22–0.91, 0.21–0.98, respectively. Nonchurch members and those without other friendships served as the reference categories). None of the individual SNI items was a reliable predictor of stroke after covariate adjustment. After adjusting for age, education, ethnicity, and BDI scores, SNI scores continued to predict stroke events (HR = 0.78; 95% CI = 0.63–0.97). However, this relationship was no longer significant after adjusting for CVD risk factors and CAD severity scores (HR = 0.82; 95% CI = 0.63–1.07).

TABLE 1. Mean ± Standard Deviation Values (Unless Otherwise Indicated) and Stroke Risk Factors Among Women Categorized by Social Network Index (SNI) Scores (n = 629)[a]

	Low SNI (n = 188)[b]	High SNI (n = 441)	p
Age	60.8 ± 10.9	56.6 ± 11.2	<.001
Race (% non-White)	19.1	14.5	.12
Percent completing high school	70.2	87.8	<.001
Beck Depression Inventory	12.4 ± 9.3	9.6 ± 7.5	<.001
Coronary artery disease severity score	14.9 ± 13.5	12.5 ± 11.9	.04
History of hypertension (%)	64.2	53.3	.04
History of diabetes (%)	28.2	20.1	.06
History of dyslipidemia (%)	56.7	50.6	.26
Smoking history (%)			
Never smoker	34	54.1	<.001
Former smoker	42	29.5	<.01
Current smoker	23.9	16.4	<.05
Waist circumference (inches)	37.7 ± 7.7	35.4 ± 6.5	<.001
Cardiovascular disease medications (%)[c]	56.7	42.0	.008
Aspirin (%)	61.1	58.5	.72
Lipid-lowering medications (%)	35.6	29.3	.41
Stroke events (n (%))	16 (8.5%)	16 (3.6%)	.006

[a] *Group differences evaluated with tests of means (t* tests) and categories (χ^2).
[b] *Low SNI scores consisted of women with a scale score of ≤6.*
[c] *Includes use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, and vasodilators.*

TABLE 2. Cox Regression Model Describing the Relationship Between Social Networks And Incident Stroke (n = 629)

Dependent Variable: Total Stroke Events	HR Estimate for Low Versus High SNI Scorers	Lower 95% CI	Upper 95% CI
Unadjusted SNI association	2.5	1.3	5.1
SNI—adjusted for demographics[a]	2.3	1.1	4.7
Adjusted for demographics and CAD risk factors[b]	2.7	1.1	6.5

HR = hazard ratio; SNI = Social Network Index; CI = confidence interval; CAD = coronary artery disease.
[a] *Includes age, education history, ethnicity, and Beck Depression Inventory scores.*
[b] *Includes diabetes, smoking, dyslipidemia and hypertension histories, waist-circumference, and CAD severity score.*

As summarized in Table 2, after including demographic variables, BDI scores, CVD risk factors, and CAD severity scores, the relationship between social networks and stroke was more stable using a dichotomized version of the SNI scores. In the latter model, more isolated women experienced strokes at more than twice the rate (HR = 2.7; 95% CI = 1.1–6.5) of those with higher SNI scores. In the final model, smoking history (HR = 3.0; 95% CI = 1.2–7.5 for current versus former or never smokers, respectively) and CAD severity scores (HR = 2.1; 95% CI = 1.2–3.9) were the only factors other than SNI scores to predict stroke events. There was no evidence of a lack of fit in the regression models. The Hosmer-Lemeshow statistic was nonsignificant ($p > .80$), indicating good fit, and the population R^2 estimate derived from the Shrunken R^2 statistic (0.11) differed only slightly from that observed in the final model including all covariates ($R^2 = 0.12$).

Figure 1 provides a possible explanation for the weaker linear versus categorical findings, suggesting that the relationship between social network scores and stroke contained a nonlinear component. Subsequent Cox regression results, however, in which we tested linear and nonlinear models

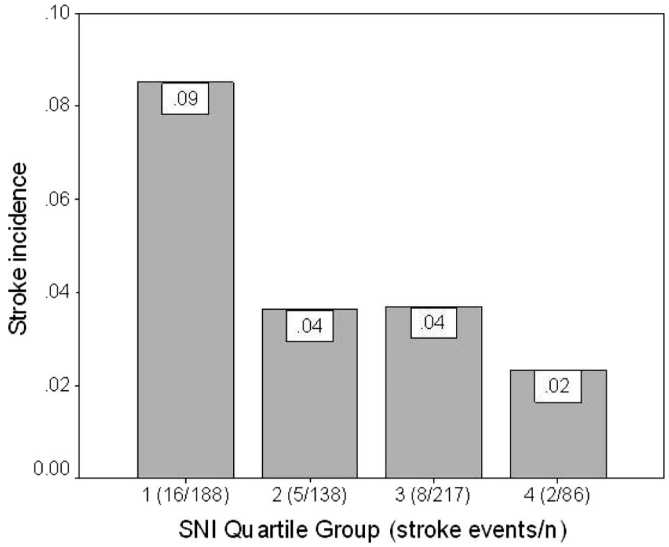

Figure 1. Stroke rates (%) across Social Network Index (SNI) quartiles (quartile values = 0–5, 6, 7–8, and >8). Group 1 represents the socially isolated women.

using a variety of nonlinear SNI transformations, failed to support this hypothesis, indicating that none of the quadratic, cubic, exponential, power, inverse, S-curve, or logarithmic transformations added to the model after controlling for the linear SNI effect.

DISCUSSION

This study is among the first to demonstrate a prospective relationship between social relationships and the risk of stroke in a clinical sample of women with suspected CAD. These results are consistent with previous studies using the SNI and other social network measures to describe the size of an individual's social circle and frequency of social contact, which have described that those reporting impoverished social relationships have an elevated risk for a variety of health events. For example, multiple population studies support an association between smaller social networks and all-cause and CVD mortality (25–28). Reduced social contacts may, at least in part, explain the well-established relationship between low socioeconomic status and health (29). Finally, social isolation is closely associated with depression, an established predictor of CVD incidence and progression (7,30,31).

To our knowledge, the relationship between social relationships and stroke has been investigated in four previous studies, with mixed results. Vogt and colleagues (16) reported social network effects on a 15-year incidence of mortality and specific disease incidence, including stroke. They described strong social network associations with mortality, but increases in stroke risk only among young participants (age range = 30–44 years), suggesting that the impact of social networks may be greater in the aftermath of disease onset. No gender-specific analyses for stroke were presented. In a study of >15,000 patients with symptoms consistent with acute myocardial infarction (32), the authors reported on relationships between living alone and short-term (30-day and 1-year) mortality and stroke events. After covariate adjustment, no relationships between living alone and mortality or stroke were present. Tomaka and colleagues (15) reported cross-sectional associations between social network and support measures and disease including stroke, observing stroke relationships with self-reported loneliness and family support. Most recently, a study of workplace stress also showed that social support was a predictor of subsequent stroke and myocardial infarction events, relationships that also held among women (14).

Combined with the current results, the above findings suggest both promise and ongoing challenges for future research in this area. The study of social relationships remains limited by a multiplicity of terminology and measurement approaches that makes it difficult to compare findings across investigations that already vary substantially in demographic and clinical characteristics. Social relationships are also highly dynamic, although few or no health studies assess these characteristics repeatedly over time, and are likely a consequence of health status changes (15,16) as well as possible cause. Our exploratory findings of single items from the SNI also suggested that the study of specific relationship subtypes beyond the standard marital status or living alone categories might also be fruitful in future research.

There are multiple behavioral and pathophysiological pathways by which social networks may affect CVD risk. Protective effects of social contacts may be due to the tangible support provided by others, emotional benefits of social relationships, by promoting physical activity (e.g., going to church, work, or a friend's place) or a combination of these and other pathways. Poor social connectedness is further associated with increased sympathetic nervous system reactivity to stress, heightened neurohormonal activation (e.g., elevated cortisol levels) and compromised immune function, which may increase susceptibility to infections and inflammation (20–22,33,34). There is currently no evidence to suggest that the mechanisms potentially linking social networks to increased stroke risk differ from those proposed to explain previously observed relationships with mortality or CAD; however, we do not believe any research has specifically addressed this point.

The WISE protocol includes a number of methodological features that improve the reliability of the social networks-stroke relationship reported here. The baseline examination included a thorough measurement of standard risk factors for CVD and psychosocial factors, use of CVD risk factor medications known to affect prognosis, and a coronary angiogram as a standardized measure of CAD severity. As a result of these design components, we were able to evaluate the predictive value of social relationships after adjusting for a number of important risk factors. In our analyses, the risk factor profiles of women with smaller social networks were consistently worse across demographic variables and CVD risk factors. Adjusting for these risk factors, however, accounted only partially for the observed SNI-stroke relationship. Our observations concerning a nonlinear trend in the relationship between SNI scores and stroke is in contrast to previous social network reports (25,27), including previous WISE data describing SNI relationships with mortality (23), which reported robust linear associations. Although it is possible that the present findings are capturing relationship elements unique to the WISE sample or methodology, the more probable explanation is that the distribution of stroke events was unstable due to the small sample. The fact that SNI scores continued to predict stroke events despite these inconsistencies reinforces the potential importance of the relationship, but the need for confirmatory research from additional studies is clear.

Study Limitations

Despite the study assets, the relationship between social networks and stroke in the WISE population is observational, and should not be misconstrued as implying a causal association. The measurement protocol does not include assessments of other speculated mechanisms linking psychosocial factors and CVD (e.g., neurohormonal activity, autonomic dysfunction, atrial fibrillation, medication and/or treatment adherence). Stroke is a broad diagnostic category, assuming several

specific diagnoses with differing etiologies that we were unable to differentiate. Stroke events occurred at a low rate in the WISE sample, and the recording of CVD events was primarily based on standardized clinical interviews rather than hospital record documentation. Although we have no evidence to suggest that our interview method was differentially biased by women with lower versus higher SNI scores, the combination of this documentation method with the small number of stroke events encourages caution. The WISE sample had a low rate of angiographically significant CAD, as substantiated by rates of obstructive coronary stenoses (>50% occlusion) present in the angiograms of <40% of participants (14), but carried a heavy disease burden as substantiated by the high rates of CVD risk factors and use of risk factor medications. Due to these characteristics, caution must be drawn in extrapolating the current findings to dissimilar populations including men, older-age samples, and asymptomatic or healthy women, among others. We measured social relationships only at baseline, whereas the size of women's social networks probably changed in multiple ways over nearly 6 years of follow-up. There is no universal definition of small social network values; we grouped women according to a median and quartile distribution of SNI scores that is unlikely to replicate perfectly in other cohorts.

Conclusion

This study demonstrates an association between social networks and incident stroke in a cohort of women with suspected CAD. Over a median 5.9 years of follow-up, more isolated women experienced a stroke rate greater than twice the rate of those with larger social networks. These findings add to an already broad literature demonstrating associations between smaller social networks and an increased risk of all-cause and CVD mortality (27,28). Although social isolation is a recognized problem in the aftermath of stroke (35), these findings suggest that social relationships may also be important to women at the stages of primary and secondary prevention.

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